

What is claimed:

1. A method of inhibiting the binding of a β -sheet fibril to RAGE on the surface of a cell which comprises contacting the cell with a binding inhibiting amount of a compound capable of inhibiting binding of the β -sheet fibril to RAGE so as to thereby inhibit binding of the β -sheet fibril to RAGE.
2. The method of claim 1, wherein the β -sheet fibril is amyloid fibril.
3. The method of claim 1, wherein the β -sheet fibril is a prion- derived fibril.
4. The method of claim 1, wherein the β -sheet fibril is selected from the group consisting of amyloid- β peptide, amylin, amyloid A, prion-derived peptide, transthyretin, cystatin C, gelsolin and a peptide capable of forming amyloid.
5. The method of claim 4, wherein the β -sheet fibril is an amyloid- β peptide is selected from the group consisting of A β (1-39), A β (1-40), A β (1-42) and A β (1-40) Dutch variant.
6. The method of claim 1, wherein the compound is sRAGE or a fragment thereof.
7. The method of claim 1, wherein the compound is an anti-RAGE antibody or portion thereof.
8. The method of claim 8, wherein the antibody is a monoclonal antibody.

9. The method of claim 8, wherein the monoclonal antibody is a human, a humanized, or a chimeric antibody.
- 5
10. The method of claim 5, wherein the compound comprises a Fab fragment of an anti-RAGE antibody.
11. The method of claim 5, wherein the compound comprises the variable domain of an anti-RAGE antibody.
- 10
12. The method of claim 5, wherein the compound comprises one or more CDR portions of an anti-RAGE antibody.
- 15
13. The method of claim 5, wherein the antibody is an IgG antibody.
14. The method of claim 1, wherein the compound comprises a peptide, peptidomimetic, a nucleic acid, or an organic compound with a molecular weight less than 500 daltons.
- 20
15. The method of claim 1, wherein the cell is present in a tissue.
16. The method of claim 15, wherein the tissue is a spleen.
- 25
17. The method of claim 15, wherein the inhibition of binding of the β -sheet fibril to RAGE has the consequence of decreasing the load of β -sheet fibril in the tissue.
- 30

18. The method of claim 16, wherein the inhibition of binding of the β -sheet fibril to RAGE has the consequence of decreasing the load of β -sheet fibril in the tissue.
- 5 19. The method of claim 1, wherein the cell is a neuronal cell, an endothelial cell, a glial cell, a microglial cell, a smooth muscle cell, a somatic cell, a bone marrow cell, a liver cell, an intestinal cell, a germ cell, a myocyte, a mononuclear phagocyte, an endothelial cell, a tumor cell, or a stem cell.
- 10 20. The method of claim 1, wherein the cell is a RAGE-transfected cell.
- 15 21. The method of claim 1, wherein the cell expresses RAGE.
- 20 22. The method of claim 1, wherein the inhibition of binding of the β -sheet fibril to RAGE has the consequence of inhibiting fibril-induced programmed cell death.
- 25 23. The method of claim 1, wherein the inhibition of binding of the β -sheet fibril to RAGE has the consequence of inhibiting fibril-induced cell stress.
- 30 24. The method of claim 23, wherein the inhibition of fibril-induced cell stress is associated with a decrease in expression of macrophage colony stimulating factor.
- 35 25. The method of claim 23, wherein the inhibition of

fibril-induced cell stress is associated with a decrease in expression of interleukin-6.

- 5 26. The method of claim 23, wherein the inhibition of fibril-induced cell stress is associated with a decrease in expression of heme oxygenase type 1.
- 10 27. The method of claim 1, wherein the cell is present in a subject and the contacting is effected by administering the compound to the subject.
28. The method of claim 27, wherein the subject is a mammal.
- 15 29. The method of claim 28, wherein the mammal is a human being.
- 20 30. The method of claim 27, wherein the administration is intralesional, intraperitoneal,, intramuscular, intravenous, liposome mediated delivery, topical, nasal, oral, anal, ocular or otic delivery.
- 25 31. A method of preventing and/or treating a disease involving β -sheet fibril formation other than Alzheimer's Disease in a subject which comprises administering to the subject a binding inhibiting amount of a compound capable of inhibiting binding of the β -sheet fibril to RAGE so as to thereby prevent and/or treat a disease involving β -sheet fibril formation other than Alzheimer's Disease in the subject.
- 30 32. The method of claim 31, wherein the compound is sRAGE or a fragment thereof.
- 35

66E F 531" e f 24 260

33. The method of claim 31, wherein the compound is an anti-RAGE antibody or portion thereof.

34. A method of determining whether a compound inhibits binding of a β -sheet fibril to RAGE on the surface of a cell which comprises:

- (a) immobilizing the β -sheet fibril on a solid matrix;
- (b) contacting the immobilized β -sheet fibril with the compound being tested and a predetermined amount of RAGE under conditions permitting binding of β -sheet fibril to RAGE in the absence of the compound;
- (c) removing any unbound compound and any unbound RAGE;
- (d) measuring the amount of RAGE which is bound to immobilized β -sheet fibril;
- (e) comparing the amount measured in step (d) with the amount measured in the absence of the compound, a decrease in the amount of RAGE bound to β -sheet fibril in the presence of the compound indicating that the compound inhibits binding of β -sheet fibril to RAGE.

35. A compound not previously known to inhibit binding of β -sheet fibril to RAGE determined to do so by the method of claim 34.

36. A method of preparing a composition which comprises determining whether a compound inhibits binding of β -sheet fibril to RAGE by the method of claim 34 and admixing the compound with a carrier.

37. A method of determining whether a compound inhibits binding of β -sheet fibril to RAGE on the surface of a cell which comprises:

- (a) contacting RAGE-transfected cells with the compound being tested under conditions

- 5 (b) removing any unbound compound;
- (c) contacting the cells with β -sheet fibril under conditions permitting binding of β -sheet fibril to RAGE in the absence of the compound;
- (d) removing any unbound β -sheet fibril;
- (e) measuring the amount of β -sheet fibril bound to the cells;
- 10 (f) separately repeating steps (c) through (e) in the absence of any compound being tested;
- (g) comparing the amount of β -sheet fibril bound to the cells from step (e) with the amount from step (f), wherein reduced binding of β -sheet fibril in the presence of the compound indicates that the compound inhibits binding of β -sheet fibril to RAGE.
- 15
38. The method of claim 37, wherein the cells are PC12 cells.
- 20
39. A compound not previously known to inhibit binding of β -sheet fibril to RAGE determined to do so by the method of claim 37.
- 25 40. A method of preparing a composition which comprises determining whether a compound inhibits binding of β -sheet fibril to RAGE by the method of claim 37 and admixing the compound with a carrier.

add a2